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ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,788	KATO ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-11,13-17 and 19* is/are pending in the application.

4a) Of the above claim(s) *11,13-17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 4/23/2008 is acknowledged and has been entered. Claim 1-5, 7, 9-10 and 11 are currently amended. Claims 8, 12 and 18 are pending. Claims 1-7, 9-11, 13-17 and 19 are pending. Claims 11, 13-17 and 19 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7, 9-10 are addressed in this Office action. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new ground(s) of rejection necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Ground(s) of Rejection

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-7, 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1 lack proper antecedent basis for the "the second strand cDNA" in step iv because no prior steps recites the production of a "second-strand cDNA". It is suggested amending the claims such that the claim language agrees,

(b) Claims 1-7, 9 and 10 are indefinite and confusing in the step iv for the "replacing the RNA in the mRNA/cDNA heteroduplex with the second strand cDNA..." because it is unclear how the cDNA "replaces" the mRNA in the heteroduplex. Further the specification does not clearly define how this replacement process occurs. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion (see *ex parte Erlich*, 3 UsPQ2d1011, p.1011 (Bd. Pat, Applicant. Int.1986). Clarification is required as to Applicant's intent.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-7, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al (5962271, citation made of record in prior Office action) in view of Mueller et al (6558927, filed May 2000). Regarding claim 1, Chenchik et al teach a method for synthesizing cDNA possessing a 5'end nucleotide cap structure, which method comprises the steps of: (i) annealing a double-stranded DNA primer and an mRNA mixture, (ii) preparing an mRNA/cDNA heteroduplex by synthesizing the first-

strand cDNA primed with the double-stranded DNA primer using reverse transcriptase, wherein the 3' end nucleotide of the first strand cDNA comprise an anchor (see for example Figure 1), (iii) circularizing the mRNA/cDNA heteroduplex by joining the 3' and 5' ends of the DNA strand containing cDNA using ligase and replacing the RNA in the mRNA/CDNA heteroduplex with the second strand cDNA thereby synthesizing the cDNA (see figure 4-1 and 4-2, col. 3-5, 7-9 and Examples; see also col. 8, line 61 to col. 9, line 13) possessing the 5' end nucleotide cap structure comprising the formula dN_1-dN_2-....dNm-rN_1-rN2....rNn, wherein dN represents a deoxyribonucleotide selected from among dAMP, dCMP, dGMP and dTMP; m represents an integer 0 and above, preferably from 10-50; rN represents a ribonucleotide selected from among AMP, CMP, GMP and UMP, preferably GMP; and n represents an integer 0 and above, preferably from 3 to 7 (col. 3, line 50 to col. 4, line 50).

Chenchik do not expressly limit the anchor of the first strand cDNA to dC(dA)n, wherein n=0-5 or wherein the double stranded cap structure is limited to DTndG, wherein n=0-5.

Mueller et al teach a method similar to that of Chenchik for the 5' cap dependent modification, cloning and/or amplification of cDNAs. Mueller et al teach that the method comprises the use of first strand cDNA comprising dC(dA)n wherein n=3-4, and wherein the second strand cDNA possesses the 5' end nucleotide of (dT)ndG, wherein n=3-4 (see col. 3, lines 4-52 and col. 4, lines 1-15). Mueller et al teach that the terminal sequence motif (5'-dC_3rA_{3-4}) formed in this manner enables the full-length cDNA to be selectively ligated to a double stranded DNA adaptor (5'-$dT_{3-4}dG_3$) using T4 ligase.

Mueller et al teach that the method leads to the specific amplification of full length cDNA which contains a complete 5' sequence of the mRNA. Mueller et al teach that subsequently a cDNA bank can be constructed after a suitable amplification by PCR (col. 4, lines 1-15). Mueller teaches that the method allows cloning or amplification of cDNAs to obtain cDNAs that have a complete 5' end in the simplest possible manner and as efficiently as possible (col. 2, lines 17-21).

Thus, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to apply the adaptor sequences comprising (5'-dC_3rA_{3-4}) and (5'-$dT_{3-4}dG_3$) at the end of the first strand cDNA and second strand cDNA as taught by Chenchik et al for the predictable result of enabling cloning or amplification of cDNAs that have a complete 5' end in the simplest possible manner and as efficiently as possible as suggested by Mueller et al. One could expect predictable results of substituting the cDNA anchor structure and/or cDNA cap structure of Mueller et al in the synthesis method of Chenchik since both arts recognize the usefulness of the cDNA structures in the synthesis of full-length cDNA having the complete sequence information of full length mRNA.

Regarding claim 2, Chenchik et al teach that the small amount of total RNA from 10-50 mg of "difficult" cells or tissues, like human biopsy tissues, pathogenic microorganisms, and tissues at different development stages and so on (col. 11, lines 32-35). One of ordinary skill in the art at the time of the claimed invention would have a reasonable expectation of success in obtaining mRNA contained in a cell extract for use in methods of synthesizing cDNA possessing a cap structured based on the teachings

of Chenchik et al. It would have been *prima facie* obvious over the cited prior arts in the absence of secondary consideration.

Regarding claim 3, Chenchik et al teach the method of claim 1, wherein mRNA possessing a cap structure is synthesized by in vitro transcription (col. 5, lines 11-53, and claim 1).

Regarding claim 4, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains a sequence complementary to a partial sequence of mRNA possessing a cap structure (see col. 7, line 52 to col. 8, line 43).

Regarding claim 5, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains an oligo dT complementary to a poly(A) sequence of mRNA possessing a cap structure (col. 7, lines 50-56).

Regarding claim 6, Chenchik et al teach the method of claim 1, wherein the ligase is T4 RNA ligase (col. 14, line 62 to col. 15, line 1).

Regarding claim 7, Chenchik et al teach the method of claim 1, which comprises the following step between the step (ii) and the step (iii): (ii') generating a 5'-protruding end or a blunt end at the terminal of the double-stranded DNA primer by cutting the conjugate of the mRNA/cDNA heteroduplex and the double-stranded DNA primer using a restriction enzyme (col. 11, Example 2).

Regarding claim 9, Chenchik et al teach wherein the double stranded DNA primer may be a linear plasmid vector which inherently comprises an origin of replication and promoter for cDNA expression (col. 7, lines 64-66). Mueller et al additionally teaches wherein the double-stranded nucleic acid molecules that are used can contain sequences which facilitate a subsequent analysis after the amplification is completed. These include promoter sequences suitable for in vitro transcription and restriction cleavage sites (col. 3, lines 13-20).

Regarding claim 10, Chenchik et al teach the method of claim 8, which further comprises the following step: (v) incorporating the double-stranded cDNA composed of the first-strand cDNA and the second-strand cDNA into a vector DNA (Figure 4 and col. 14, line 62 to col. 15, line 2).

Conclusion

7. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/cbw/

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637